Journal of Alzheimer's Disease 93 (2023) 449–457
DOI 10.3233/JAD-221252
IOS Press

Change in the Quick Dementia Rating System Across Time in Older Adults with and without Cognitive Impairment

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Handling Associate Editor: Munira Sultana

Accepted 1 March 2023
Pre-press 1 April 2023

Abstract.
Background: The Quick Dementia Rating System (QDRS) is a brief, informant-reported dementia staging tool that approximates scores on the Clinical Dementia Rating Scale in patients with Alzheimer's disease (AD).
Objective: The current study sought to examine change in the QDRS across time, which is necessary for clinical and research efforts.
Methods: One-hundred ten older adults (intact, mild cognitive impairment [MCI], mild AD, classified with Alzheimer's Disease Neuroimaging Initiative criteria) were rated on the QDRS by an informant and had an amyloid positron emission tomography scan at baseline. The informant re-rated each participant on the QDRS after one year. Dependent t-tests compared the entire sample and various subgroups (e.g., cognitive status, amyloid status) on baseline and follow-up QDRS scores.
Results: In the entire sample, the Total score on the QDRS significantly increased (i.e., worsened) on follow-up ($p < 0.001$). When subgroups were analyzed, the MCI and mild AD subjects showed increasing (i.e., worsening) QDRS Total scores (both $p < 0.001$), but the intact subjects remained stable over time ($p = 0.28$). Additionally, those classified as being amyloid positive at baseline showed significantly increased QDRS Total scores at follow-up ($p < 0.001$) compared to those who were amyloid negative at baseline, whose QDRS Total scores remained stable over time ($p = 0.63$).
Conclusion: The QDRS can potentially demonstrate worsening functioning status across one year, especially in those who have MCI or mild AD and those who are amyloid positive. Therefore, the current results preliminarily suggest that the QDRS may provide an efficient tool for tracking progression in clinical trials in AD.

Keywords: Alzheimer's disease, cognitive decline, longitudinal studies, mild cognitive impairment

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INTRODUCTION

For clinical trials in Alzheimer's disease (AD) to continue to advance, there is a need to identify and screen large numbers of potential participants [1]. Current screening methods that involve extensive cognitive batteries and advanced neuroimaging tend to be time-consuming, expensive, and may not generalize to the broader population [2]. For example, an amyloid positron emission tomography (PET) scan can only be completed in a specialized center with technologically-advanced equipment and uniquely-trained personnel, take 2–3 h to complete, and cost $3,000 or more. More effective, convenient, and less costly screening methods that identify more diverse samples in AD trials are needed [3].

The Quick Dementia Rating System (QDRS) may serve an important role as a pre-screening measure for potential participants in AD trials. This 10-item rating scale can be completed by a patient or informant (e.g., no specially-trained personnel), it is inexpensive (e.g., free for academic or non-commercial purposes with permission of its developer [although a licensing agreement is needed for clinical trials or commercial purposes]), it is efficient (e.g., takes 3–5 min to complete), and it can be remotely collected as a first step in the screening process. It has approximated scores on the Clinical Dementia Rating scale [4, 5], the gold standard in AD clinical trials [6]. It has demonstrated adequate reliability and validity [5], has been related to neuropsychological tests [5, 7], and has been linked to key biomarkers in AD [8]. The current study elected to use the informant-rated version of the QDRS for multiple reasons, including most studies validating the QDRS have utilized the informant version [9–12] and cognitively impaired individuals may lack insight [13, 14].

However, to our knowledge, no studies have tracked the QDRS across time. Therefore, the current study sought to further validate the QDRS as a screening measure for AD clinical trials by examining its change over one- and one-third years in older adults who are cognitively intact compared with amnestic mild cognitive impairment (MCI) or mild AD. It was hypothesized that the QDRS, when rated by a knowledgeable informant, would remain relatively stable in the intact participants, but demonstrate decline (i.e., increasing scores) in those with MCI and AD. We also examined change across this time period in those who were classified as being amyloid positive versus negative at baseline, and it was hypothesized that those who were amyloid positive at baseline would show worsening on the QDRS over time compared to those who were amyloid negative. Finally, changes in the QDRS were compared to changes on a cognitive screening measure, and these changes were expected to correlate. Further support for the QDRS as a clinical trial screening measure in AD might allow for its use in relevant clinical trials.

MATERIALS AND METHODS

Participants

One hundred ten older adults were recruited from a cognitive disorders clinic or through the community between 2018–2022 to participate in a study of brain imaging and neuropsychological testing across the AD spectrum. Their mean age was 74.3 (SD = 5.7, range = 65–91) years and their mean education was 16.0 (SD = 2.4, range = 12– 0) years. Most were Caucasian (99.1%) and 60% were female. Mean premorbid intellectual functioning—as measured by the Reading subtest of the Wide Range Achievement Test-4 (WRAT-4) [15]—was in the average range (M = 110.3, SD = 8.5), and self-rating of depression symptoms were minimal on the 15-item Geriatric Depression Scale (M = 1.3, SD = 1.3) [16].

Some participants were identified in the cognitive disorders' clinic via a medical records review, especially focused on any prior neuropsychological testing, to see they would likely fit into the Alzheimer's Disease Neuroimaging Initiative (ADNI) criteria for MCI or mild AD. Results of any prior neurological exams and brain imaging were also considered. Community presentations on memory and aging were conducted to solicit research volunteers, which were more likely to be cognitively intact. However, approximately 15% of amnestic MCI cases were identified in the community. Confirmation of group assignment was made with the ADNI [17] classification battery, which included the Mini-Mental Status Examination (MMSE) [18], the Clinical Dementia Rating Scale [19], and the Wechsler Memory Scale–Revised [20] Logical Memory II, with each test having cutoffs to indicate if a participant was intact or impaired.

Participants were included if they were 65 years of age or older, had a knowledgeable informant who would comment on their cognition and daily functioning, and fell into one of the groups based on ADNI classification battery. Participants were excluded for medical comorbidities likely to affect cognition (e.g., neurological conditions, current severe

depression, substance abuse, major psychiatric conditions), inability to complete MRI or PET, inability to complete cognitive assessments, and being enrolled in an anti-amyloid clinical drug trial. Additional exclusion criteria included a score of > 5 on the 15-item Geriatric Depression Scale, a Clinical Dementia Rating score of ≥ 2, or a MMSE score of < 20. Sixty-seven individuals were excluded for a variety of reasons (e.g., neurological condition = 10, unable to complete MRI = 10, did not fit into any group = 9, clinical results did not indicate AD = 9, medical condition = 8, elevated Geriatric Depression Scale = 7, psychiatric condition = 3, MMSE score of < 20 = 3, Clinical Dementia Rating score of ≥ 2 = 3, under 65 years of age = 2, allergic reaction that might interfere with PET = 2, no study partner = 1). Of the 67 individuals who were excluded from the study, nearly all were excluded during the screening process (i.e., before the first study visit). No potential participants were excluded based on race or ethnicity.

Procedure

Procedures were approved by the local Institutional Review Board. Following informed consent/assent, participants underwent testing with the ADNI battery and other neuropsychological testing at a baseline visit, which included the QDRS and MMSE. Participants returned in 37.01 days (SD = 49.7, range = 8-306) to receive amyloid PET imaging of the brain using ^{18}F-Flutemetamol. They also returned after 469.1 days (SD = 109.2, range = 360-991) for a follow-up visit to repeat the ADNI and neuropsychological batteries, as well as the QDRS and MMSE.

Measures

The QDRS [5] is a patient or informant reported dementia staging tool with 10 questions that rate the patient's functioning in memory and recall, orientation, problem-solving, activities outside the home, functioning at home, personal hygiene, behavior and personality changes, language and communication, mood, and attention. Scores range from 0 to 30, with higher scores indicating more cognitive impairment. It has two subdomains, Cognitive and Behavioral, which account for 40% and 60% of the questionnaire, respectively. Although the QDRS can be completed by either the patient or informant, in this study, informants completed this measure on their respective patients at two time points. Informants were used because most studies validating the QDRS have utilized the informant version [9–12] and cognitively impaired individuals may lack insight [13, 14].

The MMSE [18] is a widely-used cognitive screening test that assesses orientation, attention, language, construction, and memory. Scores range from 0 to 30, with higher scores indicating better cognitive abilities.

Amyloid imaging

Amyloid imaging was performed using ^{18}F-Flutemetamol (Vizamyl), which is a radioactive diagnostic agent indicated for PET imaging of the brain to estimate beta-amyloid neuritic plaque density in adult patients with cognitive impairment. ^{18}F-Flutemetamol was produced under PET cGMP standards and conducted under an approved FDA Investigational New Drug application. A GE Discovery PET/CT 710 (GE Healthcare) was used in this study. This PET/CT scanner has full width at half-maximum spatial resolution of 5.0 mm and excellent performance characteristics [21, 22]. Approximately 90 min after approximately 185 MBq (5.0 mCI) of ^{18}F-Flutemetamol was injected intravenously, a 20-min PET/CT scan of the brain was performed. Emission data was corrected using a low-dose non-diagnostic quality CT acquisition for attenuation correction of the PET emission data. Reconstructed emission images were interpreted using transaxial, coronal, and sagittal views. Images were interpreted by comparing the radioactivity in cortical gray matter cerebral cortex with activity in the adjacent white matter. Images were initially interpreted visually using the procedures outlined in the Vizamyl package insert [23]. Specifically, the following bilateral cortical regions—prefrontal, parietal, occipital, precuneus, posterior cingulate, and lateral temporal cortex—were assessed. Each scan was interpreted as positive or negative. Positive scans showed uptake in at least one cortical area (prefrontal, parietal, occipital, precuneus, posterior cingulate, and lateral temporal cortex) of the distinct gray and white matter contrast. In addition, the cortical uptake in the striatum could have also been abnormally increased. Negative scans showed a clear separation of uptake of white matter from cortical grey matter in the frontal, lateral temporal, and inferolateral parietal cortex. In addition, the expected gap between white matter in the two hemispheres is preserved in the posterior cingulate and precuneus. Images were also analyzed semi-quantitatiively, where uptake in

Table 1
Demographic information and QDRS scores for the total sample and diagnostic groups

Variable	Total Sample	Cognitively Intact	MCI	AD	Group Differences
N	110	52	31	27	
Age (y)	74.3 (5.7)	72.9 (5.1)	74.1 (5.3)	77.2 (6.4)	F=5.4, $p=0.006$ $c>$a,b
Education (y)	16.0 (2.4)	16.6 (2.2)	15.0 (2.6)	15.9 (2.4)	F=4.3, $p=0.016$ $a>$b
Sex (% female)	60.0%	61.5%	61.3%	55.6%	n.s.
Race (% Caucasian)	99.1%	100.0%	96.8%	100.0%	n.s.
Depression (raw score on GDS)	1.3 (1.3)	0.9 (1.1)	1.7 (1.6)	1.4 (1.1)	F=4.5, $p=0.01$ $b>$a,c
Total QDRS Score at baseline	3.1 (3.1)	0.5 (0.8)	4.3 (2.3)	6.6 (2.0)	F=126.5, $p<0.001$ $c>$b>a
Total QDRS Score at follow-up	4.2 (4.6)	0.6 (0.9)	5.5 (3.0)	9.7 (4.0)	F=113.2, $p<0.001$ $c>$b>a
Cognitive Subtotal at baseline	1.5 (1.5)	0.1 (0.3)	2.1 (0.8)	3.2 (1.0)	F=193.8, $p<0.001$ $c>$b>a
Cognitive Subtotal at follow-up	1.9 (2.0)	0.2 (0.4)	2.8 (1.3)	4.1 (1.6)	F=128.9, $p<0.001$ $c>$b>a
Behavioral Subtotal at baseline	1.6 (1.7)	0.4 (0.6)	2.2 (1.8)	3.4 (1.3)	F=57.7, $p<0.001$ $c>$b>a
Behavioral Subtotal at follow-up	2.3 (2.7)	0.4 (0.5)	2.7 (1.9)	5.6 (2.6)	F=88.6, $p<0.001$ $c>$b>a

AD, Alzheimer's disease; GDS, 15-item Geriatric Depression Scale, MCI, mild cognitive impairment, n.s., not significant; QDRS, Quick Dementia Rating System. In the Group Differences, a = intact, b = MCI, c = AD.

brain regions of interest were automatically generated by using the CortexID Suite analysis software (GE Healthcare). ^{18}F-Flutemetamol binding was analyzed using a regional semi-quantitative technique [24, 25]. The CortexID Suite software generates, semi-quantitative regional (prefrontal, anterior cingulate, precuneus/posterior cingulate, parietal, mesial temporal, lateral temporal, occipital, sensorimotor, cerebellar grey matter, and whole cerebellum) standardized uptake value ratios (SUVRs) normalized to the pons. A composite standardized uptake value ratio (SUVR) in the cerebral cortex was generated automatically and normalized to the pons using the CortexID Suite software [26]. Overall, Cortex ID results were reviewed to confirm the visual interpretation. When the visual and Cortex ID results were discordant, the scan was labeled equivocal.

Data analysis

To examine change in QDRS scores over approximately one- and one-third years, dependent t-tests were calculated comparing baseline scores to one-year follow-up scores in the entire sample and within each group (AD, MCI, Intact). Correlations were also calculated between baseline and follow-up scores for the entire sample and each group. Additionally, to examine change in QDRS scores by amyloid status, dependent t-tests were calculated comparing baseline scores to follow-up scores in those who were amyloid positive at baseline and those who were amyloid negative at baseline. For each analysis, the QDRS Total, Cognitive, and Behavioral scores were examined. Finally, to examine if changes on the QDRS were related to changes on the MMSE from baseline to follow-up, Pearson correlations were examined in the entire sample. To protect against multiple comparisons, a false discovery rate was calculated at 0.05.

RESULTS

As can be seen in Table 1, 52 of the participants were classified at baseline as cognitively intact, 31 were classified as amnestic MCI, and 27 were classified as AD. Demographically, those with AD were significantly older than the other two groups ($p<0.05$), and the intact individuals had significantly more years of education than those with MCI ($p=0.004$). Those with MCI rated themselves as significantly more depressed than those who were intact or had AD (F[109] = 4.5, $p=0.01$). There were no differences between the groups on sex or race, ($p>0.05$). All three groups were significantly different on the informant-rated QDRS Total score ($p<0.001$), as well as the Behavioral ($p<0.001$) and Cognitive ($p<0.001$) subdomains at

Table 2
Demographic information and QDRS scores for those classified as flutemetamol positive or negative

Variable	Flute -	Flute+	Flute differences
N	41*	65*	
Age (y)	73.1 (5.4)	75.5 (5.5)	t=-2.2, $p=0.03$
Education (y)	16.6 (2.1)	15.6 (2.6)	t=2.1, $p=0.04$
Sex (% female)	58.5%	61.5%	n.s.
Race (% Caucasian)	100%	98.5%	n.s.
Depression (raw score on GDS)	1.1 (1.2)	1.4 (1.4)	n.s
Total QDRS Score at baseline	1.0 (2.0)	4.5 (2.9)	t=-6.7, $p<0.001$
Total QDRS Score at follow-up	0.9 (1.5)	6.5 (4.6)	t=-7.6, $p<0.001$
Cognitive Subtotal at baseline	0.3 (0.7)	2.2 (1.4)	t=-8.3, $p<0.001$
Cognitive Subtotal at follow-up	0.4 (0.8)	3.0 (1.9)	t=-8.3, $p<0.001$
Behavioral Subtotal at baseline	0.7 (1.4)	2.2 (1.7)	t=-4.8, $p<0.001$
Behavioral Subtotal at follow-up	0.5 (0.8)	3.5 (2.8)	t=-6.7, $p<0.001$

*Four participants could not be classified as Flute – or+so they were excluded from these comparisons.
Flute, flutemetamol; GDS, 15-item Geriatric Depression Scale; n.s., not significant; QDRS, Quick Dementia Rating System.

both baseline and follow-up visits, with the cognitively intact participants having the lowest/best scores, followed by the MCI participants, and then the AD participants (Table 1). There were also group differences for cerebral amyloid deposition ($p<0.001$, intact < MCI, AD). Although there were differences between groups on age and education, depression, QDRS scores, and biomarkers, these differences were not controlled for in the subsequent analyses, which were within-group comparisons.

In the comparison of individuals by their amyloid status, 41 were classified as amyloid negative and 65 were classified as amyloid positive (with 4 being equivocal, who were excluded from this set of analyses). As seen in Table 2, those who were amyloid positive tended to be older, less educated, and have higher QDRS scores ($p<0.05$) than those who were classified as amyloid negative. As with the comparisons between the intact, MCI, and AD participants, these demographic and QDRS differences were not controlled for in analyses, as they were within-group comparisons.

Change in QDRS in the entire sample

For the entire sample, the Total score on the QDRS was significantly correlated between baseline and follow-up ($r=0.82$, $p<0.001$), indicating that participants retained their place within the distribution of QDRS scores from baseline to follow-up. Despite this, over the follow-up period, the Total score on the QDRS significantly increased/worsened (t[109]=-4.4, $p<0.001$) (See Table 1). This same pattern was observed for the Cognitive subtotal ($r=0.87$, $p<0.001$; t[109]=-4.7, $p<0.001$) and the Behavioral subtotal ($r=0.71$, $p<0.001$; t[109]=-3.7, $p<0.001$).

Change in QDRS in intact, MCI, and AD

The change in QDRS scores for these groups are presented in Table 1. For the intact subjects, the Total score on the QDRS was significantly correlated between baseline and follow-up ($r=0.36$, $p=0.01$), but the two subtotals only trended in this direction (Cognitive: $r=0.30$, $p=0.03$; Behavioral:r=0.26, $p=0.07$). Over the follow-up period, the Total score on the QDRS remained stable (t[51]=-0.6, $p=0.28$). Similarly, the Cognitive and Behavioral subtotals did not decline on follow-up (t[51]=-1.4, $p=0.09$) and the Behavioral subtotal (t[51] = 0.1, $p=0.46$).

For those classified as MCI at baseline, all three QDRS scores were significantly correlated at baseline and follow-up (Total: $r=0.54$, $p=0.002$; Cognitive: $r=0.69$, $p<0.001$; Behavioral: $r=0.48$, $p=0.006$). Across time, significant worsening was observed on the Total (t[30]=-2.5, $p=0.009$) and Cognitive subtotal (t[30]=-4.0, $p<0.001$) scores of the QDRS, but not on the Behavioral subtotal (t[30]=-1.5, $p=0.07$).

For those classified as AD at baseline, the three QDRS scores were not significantly correlated between baseline and follow-up (Total: $r=0.34$, $p=0.082$; Cognitive: $r=0.38$, $p=0.054$; Behavioral: $r=0.24$, $p=0.22$), indicating that individuals moved around in the distribution of scores from baseline to follow-up. Despite this, significant worsening was observed on the Total (t[26]=-4.2, $p<0.001$) and Cognitive (t[26]=-3.0, $p=0.005$) Behavioral subtotal (t[26]=-4.4, $p<0.001$) scores of the QDRS.

Change in QDRS in amyloid positive and negative

The change in QDRS scores for these groups are presented in Table 2. For those classified as amyloid negative at baseline, the Total score on the QDRS was significantly correlated between baseline and follow-up ($r = 0.76$, $p < 0.001$), as were the two subtotals (Cognitive: $r = 0.78$, $p < 0.001$; Behavioral: $r = 0.68$, $p < 0.001$), indicating that individuals maintained their respective places within the distribution of scores at baseline and follow-up. Over the follow-up period, the Total score on the QDRS remained stable (t[40] = 0.51, $p = 0.63$). Similarly, the Cognitive and Behavioral subtotals did not significantly change on follow-up (Cognitive: t[40]=-1.1, $p = 0.28$; Behavioral: t[40] = 1.2, $p = 0.25$).

For those classified as amyloid positive at baseline, all three QDRS scores were significantly correlated at baseline and follow-up (Total: $r = 0.75$, $p < 0.001$; Cognitive: $r = 0.78$, $p < 0.001$; Behavioral: $r = 0.65$, $p < 0.001$), again indicating consistency of scores within the baseline and follow-up distributions. Despite this, across time, significant worsening was also observed on the Total (t[40]=-5.3, $p < 0.001$), Cognitive subtotal (t[64]=-5.0, $p < 0.001$), and Behavioral subtotal (t[64]=-4.8, $p < 0.001$) of the QDRS for this group.

Since there was a notable confound between cognitive status and amyloid status (i.e., those with cognitive impairment were more likely to be amyloid positive), correlations and dependent t-tests were also examined between QDRS scores at baseline and follow-up for only the cognitively intact participants. Such analyses might suggest if the QDRS could be used in disease-modifying treatment trials, where individuals are likely to be cognitively healthy but biomarker positive. In the 38 intact participants classified as amyloid negative at baseline, the three QDRS scores were not significantly correlated between baseline and follow-up ($p > 0.05$), and minimal changes occurred on the QDRS scores from baseline to follow-up ($p > 0.05$, $d = 0.04$–0.20). In the 11 intact participants classified as amyloid positive at baseline, the Cognitive subtotal was significantly correlated between baseline and follow-up (r[10] = 0.78, $p = 0.004$), but the Total and Behavioral subtotal were not. Similarly, a trend for increasing/worsening scores were seen on the Cognitive subtotal from baseline to follow-up (t[10]=-2.39, $p = 0.04$, $d = 0.72$), but not on the Total or Behavioral subtotal.

Change in QDRS and change in MMSE

In the entire sample, the difference score of the Total QDRS from baseline to follow-up (i.e., QDRS follow-up – QDRS baseline) was significantly and negatively correlated with the difference score of the MMSE (i.e., MMSE follow-up – MMSE baseline), such that increasing/worsening scores on the QDRS were associated with decreasing/worsening scores on the MMSE (r[109]=-0.29, $p = 0.002$). Similarly, the difference score on the MMSE was significantly and negatively correlated with the two subtotals: Cognitive (r[109]=-0.28, $p = 0.003$) and Behavioral (r[109]=-0.27, $p = 0.005$).

DISCUSSION

Although the QDRS has been related to scores on the Clinical Dementia Rating scale, neuropsychological test scores, and biomarkers of AD, no studies have reported on how QDRS scores change across time, which is crucial for its application in clinical and research settings. The current study examined how the informant-rated QDRS changed over one- and one-third years in a sample of older adults who are cognitively intact or have amnestic MCI or or mild AD. Consistent with our hypotheses, Total scores on the informant-rated QDRS remained stable over one- and one-third years in the participants classified as intact at baseline. Conversely, in those individuals classified as MCI and mild AD over this same time period, there was significantly worsening. This pattern of change was also largely seen on the two subscales of the QDRS, especially on the Cognitive subscale. To our knowledge, this is the first study to investigate the change on the QDRS over time, and it further validates this instrument as part of the screening and tracking process for clinical trials in AD.

Cross-sectional changes have been reported on the QDRS, with cognitively intact individuals showing lower (i.e., less impaired) scores on the QDRS than cognitively impaired individuals [5, 7, 8]. For example, using a larger group of this same cohort, Duff et al. [8] noted that intact individuals scored < 1 on the Total QDRS at baseline, where individuals with MCI and AD scored much higher (means of 4 and 7, respectively) at baseline. However, these cross-sectional results provide little information about how much QDRS scores change within the same individuals over known periods of time, like six months or

one year. Longitudinal results, like in this study, can allow clinicians and researchers to better understand how much change is typical in these groups and if an individual is progressing over time. For example, for intact individuals, practically no change was observed over one year (1/10 of a point on the Total QDRS). Conversely, those with MCI worsened by more than one point, and those with mild AD worsened by over three points. Also of note is the higher level of variability in QDRS scores across time in the two impaired groups compared to the intact individuals. For example, the standard deviations at baseline for the MCI and AD groups were double that of the intact group on the Total QDRS Score, and this increased to three- and four-fold on follow-up. This variability in QDRS scores may indicate the variability within these conditions, including those who do not progress, those who progress slowly, those who progress quickly, and even those who revert. Such findings allow us to better understand the natural course of individuals on the QDRS, which could also be used to examine individual trajectories in disease-modifying clinical trials.

To further validate the value of examining change on the QDRS over time, the sample was recategorized based on their baseline amyloid PET scan as either "negative" (e.g., clear separation of uptake of white matter from cortical grey matter regions) or "positive" (e.g., uptake in at least one cortical area of the distinct gray and white matter contrast). Although Duff et al. [8] had previously reported that QDRS scores were positively correlated with amyloid deposition (i.e., higher QDRS scores being associated with greater amyloid deposition), the current analyses considered change on the QDRS across time. In individuals who showed normal amounts and distribution of uptake of ^{18}F-Flutemetamol, they did not significantly change on the QDRS over one- and one-third years. Conversely, those who showed excessive amounts and distribution of uptake of ^{18}F-Flutemetamol at baseline presented with significantly higher (i.e., impaired) QDRS scores at baseline and they significantly worsened over the course of this study. Even though the amyloid "positive" individuals were also more likely to have a diagnosis of MCI or AD, these results preliminarily support the use of the QDRS as a tracking measure in studies examining individuals who present with excessive brain amyloid. When only those who were cognitively intact were considered, there was a trend (and moderate effect size) of increasing/worsening scores on the QDRS Cognitive subtotal in the amyloid positive participants, where that was not observed in the amyloid negative individuals. Although very preliminary, such results might point to the potential value of the QDRS in disease-modifying treatment trials.

Changes on the QDRS in the entire sample was also significantly and negatively related to changes on the MMSE, a widely-used cognitive screening measure. As individuals' cognitive functioning worsened over time on the MMSE, their informants rated them as more impaired on the QDRS. Such findings are consistent with cross-sectional studies that have found relationships between the QDRS and other neuropsychological tests [5, 7]. Although the correlations were relatively small, this may have been limited by the cutoff of < 20 applied to the MMSE for participants in the current study.

This study has limitations. First, the sample was largely Caucasian and well-educated, which could limit the generalizability of these findings to more diverse populations. Second, individuals with notable depression were excluded from the study, so it is unclear if these results would remain in a more depressed sample. Third, ADNI criteria were used to classify these participants as intact, MCI, or AD, and ADNI criteria may not reflect clinical practice. Additionally, the sample sizes for the MCI and mild AD groups were relatively small, which could limit the generalizability of these results to their respective populations. It is also unclear how these results would generalize to more advanced AD or non-AD neurodegenerative conditions (e.g., Lewy body dementia, vascular dementia). Finally, the informant version of the QDRS was used in the current study, and it is unclear if the results would be similar if the participant rated him/herself. This may also be a limitation for the use of QDRS, as some mildly impaired individuals present to clinic or research visits alone. However, this limitation might be mitigated by the use of telephone- or internet-administered versions [12]. Informants pose their own challenges to this type of research, as individual differences of the informant (e.g., familiarity with the participant, timing of the assessment, emotional state of the informant) may have led to different results in this study. Despite these limitations, the current results provide additional preliminary support for using the QDRS in clinical and research evaluations of older adults with suspected AD, as well as a potential tracking measure in AD clinical trials. Making clinical trials safer, less expensive, and more efficient should be a goal of all involved in these trials.

ACKNOWLEDGMENTS

The authors have no acknowledgments to report.

FUNDING

The project described was supported by research grants from the National Institutes on Aging: R01AG055428, and it was registered at clinicaltrials.gov (NCT03466736). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institute on Aging or the National Institutes of Health. This project also utilized REDCap, which is supported by 8UL1TR000105 (formerly UL1RR025764) NCATS/NIH.

CONFLICT OF INTEREST

There are no conflicts of interest to report.

DATA AVAILABILITY

Deidentified data from this paper may be obtained by contacting the corresponding author after completing a data transfer agreement and having an approved protocol with one's local institutional review board.

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